

**This is an electronic reprint of the original article.  
This reprint *may differ* from the original in pagination and typographic detail.**

**Author(s):** Ihalainen, Johanna; Peltonen, Heikki; Paulsen, Göran; Ahtiainen, Juha; Taipale, Ritva; Hämäläinen, Mari; Moilanen, Eeva; Mero, Antti

**Title:** Inflammation status of healthy young men : initial and specific responses to resistance training

**Year:** 2018

**Version:**

**Please cite the original version:**

Ihalainen, J., Peltonen, H., Paulsen, G., Ahtiainen, J., Taipale, R., Hämäläinen, M., Moilanen, E., & Mero, A. (2018). Inflammation status of healthy young men : initial and specific responses to resistance training. *Applied Physiology, Nutrition and Metabolism*, 43(3), 252-258. <https://doi.org/10.1139/apnm-2017-0315>

All material supplied via JYX is protected by copyright and other intellectual property rights, and duplication or sale of all or part of any of the repository collections is not permitted, except that material may be duplicated by you for your research use or educational purposes in electronic or print form. You must obtain permission for any other use. Electronic or print copies may not be offered, whether for sale or otherwise to anyone who is not an authorised user.

## Manuscript Applied Physiology, Nutrition, and Metabolism

### INFLAMMATION STATUS OF HEALTHY YOUNG MEN: INITIAL AND SPECIFIC RESPONSES TO RESISTANCE TRAINING

Ihalainen Johanna K.<sup>1</sup>, Peltonen Heikki<sup>1</sup>, Paulsen Göran<sup>2,3</sup>, Ahtiainen Juha P<sup>1</sup>, Taipale Ritva S.<sup>1,4</sup>, Hämäläinen Mari<sup>5</sup>, Moilanen Eeva<sup>5</sup>, Mero Antti A.<sup>1</sup>

<sup>1</sup>*Biology of Physical Activity, Faculty of Sport and Health Sciences, University of Jyväskylä, Finland*

<sup>2</sup>*The Norwegian Olympic and Paralympic Committee and Confederation of Sports, Oslo, Norway*

<sup>3</sup>*Norwegian School of Sport Sciences, Oslo, Norway*

<sup>4</sup>*Kajaani University of Applied Sciences, Kajaani, Finland*

<sup>5</sup>*The Immunopharmacology Research Group, Faculty of Medicine and Life Sciences, University of Tampere and Tampere University Hospital, Tampere, Finland*

Correspondence to:                   Johanna K. Ihalainen, MSc  
  Biology of Physical Activity  
  University of Jyväskylä  
  P.O Box 35  
  40014 Jyväskylä, Finland  
  Tel. 358-40-8347106  
  Fax 358-14-2602071  
  Email: [johanna.k.ihalainen@jyu.fi](mailto:johanna.k.ihalainen@jyu.fi)

**Email addresses of the other authors :** Peltonen Heikki ([heikki.peltonen@jyu.fi](mailto:heikki.peltonen@jyu.fi)); Paulsen, Göran ([Goran.Paulsen@olympiatoppen.no](mailto:Goran.Paulsen@olympiatoppen.no)); Ahtiainen Juha ([juha.ahtiainen@jyu.fi](mailto:juha.ahtiainen@jyu.fi)); Taipale Ritva ([Ritva.Taipale@kamk.fi](mailto:Ritva.Taipale@kamk.fi)); Hämäläinen Mari ([Mari.Hamalainen@uta.fi](mailto:Mari.Hamalainen@uta.fi)); Moilanen Eeva ([eeva.moilanen@uta.fi](mailto:eeva.moilanen@uta.fi)); Mero Antti A. ([antti.a.mero@jyu.fi](mailto:antti.a.mero@jyu.fi))

## Abstract

**Purpose:** Our primary aim was to study the effects of a 4 wk preparatory resistance training (RT) period followed by 12 wks of two specific RT protocols (either hypertrophic-strength, HS, or strength-hypertrophy-power, SHP, training) on inflammation markers and the possible relationship of the changes in abdominal fat and lean mass to the changes in inflammation status.

**Methods:** A total of 82 healthy men were included in the study. Maximal concentric leg press strength (1RM), total body lean mass, total body and abdominal fat mass, circulating high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), interleukin-1 receptor antagonist (IL-1ra), monocyte chemoattractant protein 1 (MCP-1), and selected adipocytokines (resistin, adiponectin and leptin) concentrations were measured before (PRE) and after 4 (wk4) and 16 weeks (wk16) of RT.

**Results:** After the initial phase of RT, on wk4, abdominal and total fat mass as well as plasma leptin concentrations were significantly reduced ( $p<0.05$ ), whereas muscle mass, IL-1ra, resistin and MCP-1 concentrations were significantly increased ( $p<0.05$ ). During specialized training phase, at wk16, only HS led to further reduction in abdominal and total fat mass, resistin, and leptin ( $p<0.05$ ), whereas both training modes led to lower MCP-1 concentrations ( $p<0.05$ ).

**Conclusion:** Abdominal fat mass and circulating leptin were reduced already after 4 wks of RT. Simultaneously, circulating MCP-1 and resistin concentrations increased, possibly as markers of muscle adaptation and regeneration. The present findings also suggest that RT with hypertrophic focus is beneficial for further reductions in abdominal fat mass and to decrease circulating inflammatory markers.

**Keywords:** lean mass, muscle strengthening, adipokines, cytokines, body mass maintenance

## Introduction

Systemic inflammation is an independent risk factor for several diseases like type 2 diabetes (Pradhan et al. 2001) and atherosclerosis (Hansson 2005). Resistance training (RT) has been associated with improvements in inflammation state in overweight adults (Olson et al. 2007), elderly people (Phillips et al. 2012) as well as in specific patient groups (Conraads et al. 2002, Moraes et al. 2014). Suppressing chronic inflammation at an early stage in life via regular exercise could serve as an efficient approach to prevent or delay the onset of inflammation and related diseases (Forti et al. 2017). There is recent evidence that RT could also have beneficial effects on inflammation in untrained young men (Forti et al. 2017), however, this has not been consistent between all studies (Ara et al. 2006, Libardi et al. 2012, Rall et al. 1996).

A bout of heavy resistance exercise (RE) triggers a transient inflammatory response comprising of an augmented white blood cell count and stimulation of pro- and anti-inflammatory cytokine production (Freidenreich and Volek 2012). The cytokine response induced by a bout of heavy resistance exercise involves enhanced production of pro-inflammatory cytokines, such as interleukin-6 (IL-6) and interleukin-1 $\beta$  (IL-1 $\beta$ ). In addition to its pro-inflammatory and metabolic activities, IL-6 produced by the exercising muscle has been proposed to have anti-inflammatory properties through its stimulatory effects on the production of anti-inflammatory cytokines interleukin-1 receptor antagonist (IL-1ra) and interleukin-10 (IL-10). These mediators play a crucial role in the containment and resolution of inflammatory processes, and have been suggested to have a role in mediating the beneficial immune-modulating effects of resistance exercise (Petersen and Pedersen 2005). It has been suggested that not only the initial response to unfamiliar RE differs from the later responses but also that RT significantly affects the acute inflammation response to RE and modifies it into an anti-inflammatory direction (Ihalainen et al. 2017, Murton et al. 2014). Thus, it could be possible that the initial phase of RT in untrained participants might also induce different effects on inflammation status that have been observed in long-term RT studies.

Another mechanism explaining the anti-inflammatory effects of exercise, observed as lower circulating inflammation markers, is suggested to be the reduction in visceral fat mass with a subsequent decrease in

release of proinflammatory adipocytokines and increase in the release of anti-inflammatory adipocytokines (Gleeson et al. 2011, Robinson and Graham 2004). Adipocytokines (e.g. leptin, adiponectin, and resistin) are hormones that were first discovered to be secreted by adipose tissue and to regulate energy metabolism and appetite. More recent findings on the ubiquitous expression of their receptors and cellular effects have revealed that they also are involved in the regulation of a variety of biological functions related to immune responses and inflammatory diseases (Ouchi et al. 2011, Cao 2014, Scotece et al. 2014). A single resistance exercise bout has been demonstrated to exert specific acute effects on adipocytokine levels and the response appears to be dependent on the duration of the exercise as well as on energy expenditure (Bouassida et al. 2010, Ihalainen et al. 2014).

RT has been shown to have a positive effect on several inflammation markers, including adiponectin (Fatouros et al. 2009). However, the time course, the effects of starting RT and the effects of different RT regimens on inflammation markers are not fully understood. Consequently, our primary aim was to study the effects of 4 wk preparatory RT period followed by 12 wks of either hypertrophic-strength (HS) or strength-hypertrophy-power (SHP) RT on inflammatory markers in previously untrained men. As a secondary purpose, we evaluated the association between the changes in abdominal fat mass, total body lean mass, and strength performance variables and the selected inflammation markers. We hypothesized that both the preparatory and the more specific RT would induce significant improvements in inflammation markers and that the magnitude of these adaptations would be related to the protocol used in longer-term RT and to the changes in body composition.

## Materials and methods

**Participants.** A total of 150 men contacted us to express their interest in the study. Of these, 92 men met the participation criteria and participated in pre-measurements. The participants were randomly assigned to hypertrophy-strength training (HS, n=44) or to strength-hypertrophy-power training (SHP, n=44). In addition, 14 men served as a control group. The number of the participants that completed pre-, 4wk, and 16wk measurements and were included in this study were HS = 37 and SHP = 31. All participants reported taking part in sport activities on a weekly basis, but none were competitive athletes or had a background in systematic strength training. Participants filled in a health questionnaire prior to participation in the study. A completed health questionnaire and resting ECG were reviewed by a physician prior to exercise testing and training. All subjects reported that they were free from injury, and were not using any medications or smoking. The subjects were informed about the importance of maintaining their previous dietary habits throughout the study. Each subject was informed of the potential risks and discomforts associated with the measurements, and all of the subjects gave their written informed consent to participate. The study was conducted according to the Declaration of Helsinki, and the Ethics Committee of the University of Jyväskylä, approved the study.

**Study design.** The duration of the whole training intervention was 16 weeks. Measurements were performed prior to (wk0), after 4 weeks of preparatory RT (wk4), and after 12 weeks of specialized RT at week 16 (wk16) of training. The control group was measured only before and after the RT as a follow-up.

**Training.** The intervention started with 4 weeks of progressive muscle endurance training twice a week as one group (HS+SHP). A total of 8 training sessions were done during this initial phase RT. The participants used eight to ten exercises in one workout, 2–3 sets of every exercise, and 10–15 repetition in every set. Recovery time between the sets lasted two minutes. Training loads were 50–80 % of one repetition maximum (1 RM) increasing throughout the preparatory phase. Bilateral leg press, bilateral knee extension, and bilateral knee flexion exercises were performed with weight-stack devices during each RT session. The preparatory RT period also included exercises for the other main muscle groups of the body and were conducted once a week using machines. Chest and shoulders, upper back, trunk extensors and flexors, and

upper arms rotated during 2 weekly exercises. After 4 weeks of training, the subjects were divided into two different RT regimens: 1) training aiming especially for muscle hypertrophy and strength (HS) and 2) training aiming for muscle strength, hypertrophy and power (SHP) for 12 weeks. A total of 28 training sessions were undertaken during this specialized training phase. Participant had 2 or 3 training sessions a week, depending on the phase of the training period. The exercises used were the same as those used in the 4 wk preparatory phase. The specific RT programs performed over the next 12 wks was periodized and thus divided further into three different blocks. Every block consisted of 4 wks of RT. In the first block, the SHP group had 25 % power-strength (PS) and 75 % maximal-strength (MS) training sessions, in the second block 75 % PS and 25 % MS training sessions, and in the last block 87.5 % PS and 12.5 % MS training sessions. In contrast, the HS training group's first block consisted of 100 % HS sessions, the second block 75 % HS and 25 % MS training sessions, and the last block 25 % HS and 75 % MS training sessions. HS training contained mainly of sets including 8–12 repetitions with 75–85 % loads of 1 RM. MS training in both RT regimens consisted of neural enhancing RT with lower repetitions per set (typically 4–6) and higher intensity (86–95 % 1 RM), but also more traditional hypertrophy sets to increase muscle size. PS training consisted of sets with lower loads of 1 RM (50–80 % 1 RM) performed with maximal concentric speed. The individual loads were determined by strength testing for each exercise every fourth wk. The training techniques were carefully supervised and the training was controlled throughout the whole RT period. The sets were conducted such that the last repetition could still be performed with good technique or until concentric failure. The exception to this was the power-strength (PS) sets in SHP that were conducted with maximal concentric speed and, thus, not close to concentric failure. The training program has been described in detail by Hulmi et al. (Hulmi, Laakso, Mero et al. 2015). Subjects were advised to continue their normal recreational physical activities such as low-intensity walking, skiing, cycling, and swimming throughout the study.

**Abdominal fat.** Whole body composition was estimated by Dual X-ray Absorptiometry (LUNAR Prodigy, GE Medical Systems, Madison, USA). The DXA-scans were performed in the morning with the participant in a fasted (12 h) state. Automatic analyses (Encore-software, version 14.10.022) provided total body fat mass and total body lean mass. Abdominal fat was calculated manually defining a range of interest confined cranially by the upper end plate of the first lumbar vertebra, laterally by the ribs and caudally by

the iliac crest (Tallroth et al. 2013) at wk0. This customized range was then copied to the DXA scans at wk4 and wk16, respectively.

**Nutrition.** Subjects kept 4-day food diaries during the second block of the 12-week RT period. The researchers gave subjects both verbal and written nutritional recommendations based on the Finnish Nutrition Recommendations 2014 in a one two-hour lecture. As a rule, these follow the recommendations for the Nordic countries in Europe published in Autumn 2013 (NNR2012) and are very close to USDA and HHS dietary guidelines (2010) for normal healthy adults. The subjects were instructed on how to report nutritional intake in the diaries. During the intervention subjects were randomly given a post-workout supplement. One group received protein, one group carbohydrate, and one group protein plus carbohydrate. Protein and carbohydrates were provided by Northforce (Kuusamon Juusto Oy, Kuusamo, Finland). The protein group received 37.5 grams of whey concentrate (30 g of whey proteins, 5 g of lactose < 1 g of fat) and the carbohydrate group received 34.5 grams of maltodextrin. In contrast, the protein plus carbohydrate group received 37.5 grams of whey concentrate (30 g of whey proteins) and 34.5 grams of maltodextrin. The nutritional subgroups were randomly assigned and evenly distributed within the training groups. Nutrients provided by the supplements were included in the analysis. The food diaries were analyzed by nutrient analysis software (Nutri-Flow; Flow-team Oy, Oulu, Finland).

**Maximal-strength performance.** Maximal strength was measured by a one-repetition maximum (1RM) test of dynamic leg press exercise performed using David D210 leg press device (David Health Solutions Ltd., Helsinki, Finland). The starting position (flexed) was at a knee angle of 60 degrees, and 1RM was accepted as the highest load that the subjects could lift to a full knee extension (180 degrees). Subjects performed 3 warm-up sets and 3 to 5 trials, after which the highest load was accepted as the 1RM.

**Venous blood samples.** Fasting samples were taken in the morning (7:00-9:00 a.m.) after a 12 h overnight fast. Participants were instructed to abstain from strenuous physical activity, including RT sessions in the training programme, for 48 h before the blood samples were taken at wk0, wk4 and wk16. Venous blood samples were drawn from an antecubital vein using standard procedures and the blood was transferred into serum and EDTA tubes (Venosafe, Terumo, Belgium). The serum samples were held for 15 min at room temperature before being centrifuged for 10 min at 2000 x g (Megafuge 1.0 R, Heraeus, Germany). The EDTA-treated samples were centrifuged for 10 min at +4°C with 2000 x g (Megafuge 1.0 R, Heraeus,



Germany). Both plasma and serum were kept at  $-80^{\circ}\text{C}$  until analysed. High-sensitivity C - reactive protein (hsCRP) in serum samples was analysed by using the Immulite 1000 and immunoassay kits (Immulite, Siemens, IL, USA). The detection limit and inter-assay coefficient of variation was  $0.1\text{ g}\cdot\text{mL}^{-1}$  and 10 %, respectively. Concentrations of interleukin-6 (IL-6), monocyte chemoattractant protein-1 (MCP-1), interleukin-1 receptor antagonist (IL-1ra), adiponectin, leptin and, resistin in plasma samples were determined by enzyme-linked immunosorbent assay (ELISA) with commercial reagents (R&D Systems, Europe Ltd, Abingdon, UK). The detection limits and inter-assay coefficients of variation, respectively, were  $0.2\text{ pg}\cdot\text{mL}^{-1}$  and 7.8 % for IL-6,  $3.9\text{ pg}\cdot\text{mL}^{-1}$  and 6.5 % for MCP-1,  $15.6\text{ pg}\cdot\text{mL}^{-1}$  and 4.1 % for IL-1ra,  $19.5\text{ pg}\cdot\text{mL}^{-1}$  and 4.4 % for adiponectin,  $15.6\text{ pg}\cdot\text{mL}^{-1}$  and 6.0 % for resistin and  $15.6\text{ pg}\cdot\text{mL}^{-1}$  and 3.2 % for leptin.

**Statistical analyses.** All data are expressed as means  $\pm$  SD, except where indicated. Data was analysed using PASW statistic 22.0 (SPSS, Chicago, IL, USA). The final analysis for the present study was performed only on adherent participants (90 % adherent to exercise intervention) with outliers ( $n=3$ ) removed. Outliers were defined as a variable greater than 3 SD above the mean for wk0, wk4 or wk16. Results were similar when the same analysis was performed with outliers included. Before applying further statistical methods, the data was checked for sphericity and normality. If a specific variable violated the assumptions of parametric tests, log-transformation was used. This concerned values of adiponectin, leptin, IL-6, MCP-1 and hs-CRP. Absolute changes were analysed via two-way repeated analysis of variance for main (time and group) and interaction (group  $\times$  time) effects. For each analysis, the corresponding baseline values and the nutritional supplement were used as a covariate when appropriate. If a significant main effect or interaction was observed, the change from wk0-values for mid and from wk4 to post were compared between groups using paired t-tests with Bonferroni correction. Effect sizes (ES) are given as Cohens d with an effect size of 0.20-0.50 being considered small, 0.50-0.80 medium, and  $>0.80$  large. Spearman's correlation coefficients were used to examine the associations between depending variables. The level of statistical significance was set at  $p < 0.05$ .

## Results

**Training adherence.** The training adherence was  $99\pm 2\%$  and  $95\pm 1\%$  in HS and SHP groups, respectively.

All subjects completed at least 90% of the overall training volume.

**Nutrition.** Total energy intake (MJ) was  $10.1 \pm 1.8$  and  $11.2 \pm 2.1$  in HS and SHP groups, respectively.

There was no significant difference in dietary intake between the groups.

**Inflammation markers.** Effects of RT on the circulating levels of inflammatory markers are shown in Table 1. There were no significant differences in the initial 4wk RT phase responses between the HS and SHP groups in any of the inflammation markers. All the variables stayed statistically unaltered in the control group (C) after the follow-up.

\*\*Table 1 somewhere here\*\*

IL-6, CRP, and adiponectin concentrations remained unaltered by RT. Interesting statistically significant alterations were observed in IL-1ra, MCP-1, resistin, and leptin (Figure 1). A significant increase in IL-1ra concentration was observed after the initial phase of RT ( $p < 0.001$ , ES = 0.989). The specialized RT phase did not have any additional effect on IL-1ra. MCP-1 concentration increased after the initial phase of RT ( $p = 0.039$ , ES = 0.548), however, both HS and SHP had a significant lowering effect on MCP-1 levels ( $p = 0.045$ , ES = 0.522;  $p = 0.027$ , ES = 0.604, respectively). In the initial phase of RT, circulating resistin concentrations increased significantly ( $1.25 \pm 0.40\%$ ;  $p = 0.039$ , ES = 0.546) but were reduced during the following 12 wks of HS training ( $p = 0.046$ , ES = 0.519). Significant changes in circulating leptin concentrations were observed after the initial 4 wk phase of RT ( $p = 0.006$ , ES = 0.799) and it was further reduced during the specialized HS training period ( $p = 0.037$ , ES = 0.538). SHP had no effect on leptin ( $p = 0.821$ ).

\*\*\*Figure 1 somewhere here\*\*\*

**Total and abdominal fat mass.** Changes in body composition and 1RM are summarized in Table 2. No significant changes were observed in body mass. We observed a significant reduction in total fat mass from wk0 to wk4 ( $-3.2 \pm 6.8 \%$ ,  $p = 0.001$ ,  $ES = 0.969$ ). During the specialized training period a significant group  $\times$  time interaction was observed ( $p = 0.006$ ,  $ES=0.795$ ) in total fat mass. Thus, from wk4 to wk16 we observed a significant reduction in total fat mass only in the HS group ( $-6.2 \pm 10 \%$ ,  $p < 0.001$ ,  $ES = 0.993$ ). In line with the reduction in total fat mass, abdominal fat mass was significantly reduced after 4wk of RT ( $p=0.001$ ) and a significant group  $\times$  time interaction was observed ( $p = 0.004$ ,  $ES = 0.848$ ) in abdominal fat mass after specialized training. Abdominal fat mass decreased significantly ( $-7.9 \pm 11.4 \%$ ,  $p < 0.001$ ,  $ES = 1.00$ ), in HS only. Significant changes in total and abdominal fat mass were not observed in the SHP group after specialized training ( $0.1 \pm 6.6 \%$  and  $3.3 \pm 9.4 \%$ , respectively). In the C group a significant increase in total fat mass was observed ( $+8 \pm 22 \%$ ,  $p = 0.018$ ).

**Lean mass.** Lean mass increased significantly from wk0 to wk4 ( $1.4 \pm 1.9 \%$ ,  $p = 0.001$ ,  $ES = 1.00$ ), and a significant group  $\times$  time interaction was observed during the specialized RT ( $p = 0.041$ ,  $ES = 0.536$ ). A significant increase in lean mass was observed from wk4 to wk16 both in both HS and SHP groups ( $1.3 \pm 1.9 \%$ ,  $p < 0.001$ ,  $ES = 1.00$ ;  $1.5 \pm 1.7 \%$   $p = 0.018$ ,  $ES = 0.669$ , respectively) but the increase was greater in HS.

**1RM.** A significant main effect of time was observed in 1RM from PRE to wk4 ( $p=0.001$ ,  $ES = 0.916$ ) as an increased 1RM was observed from PRE to wk4 ( $17.6 \pm 18.3 \%$ ,  $p < 0.001$ ,  $ES = 1.00$ ). Both HS and SHP training increased 1RM from wk4 to **wk16** ( $13 \pm 8.1 \%$ ,  $p < 0.001$ ,  $ES = 1.00$ ;  $11 \pm 6.5 \%$ ,  $p < 0.001$ ,  $ES = 1.00$ , respectively). 1RM did not change significantly in the control group ( $p = 0.399$ ).

\*\*\*Table 2 here somewhere\*\*\*

**Associations between changes in 1RM, body composition and inflammatory markers.** At wk0 measurements circulating leptin concentration showed a strong positive correlation with total fat mass ( $R = 0.843$ ,  $p < 0.001$ ) and abdominal fat mass ( $R = 0.775$ ,  $p < 0.001$ ) when all the subjects were pooled. In

addition, in the pooled data circulating adiponectin correlated negatively with 1RM ( $R = 0.355$ ,  $p=0.001$ ) and IL-6 had a weak positive correlation with abdominal fat mass ( $R = 0.263$ ,  $p = 0.024$ ). The greater reduction in fat mass was associated with greater reduction in circulating leptin concentration. As in the initial phase of RT when the groups are pooled, the change in total fat mass and abdominal fat mass correlated significantly with the change in circulating leptin concentrations ( $R=0.406$ ,  $p<0.001$ ;  $R=0.391$ ,  $p<0.001$ , respectively). The same was observed during specialized training as the change in circulating leptin concentrations correlated with the change in abdominal fat mass as well as with the change in total fat mass ( $R = 0.363$ ,  $p=0.004$ ;  $R = 0.539$ ,  $p<0.001$ , respectively). The greater increase in muscle mass was associated with a reduction in circulating adiponectin concentrations. As in the pooled data, an inverse relationship between the change in concentration of circulating adiponectin and the change in total lean mass from wk4 to wk16 was observed ( $R = -0.255$ ,  $p = 0.039$ ).

## Discussion

The present study assessed the effects of RT on inflammatory markers, i.e., cytokines and adipocytokines, in previously untrained men. The unique aspect of the present study was the design with an initial preparatory phase of RT, comprising of muscle endurance type of RT, followed by either hypertrophy-strength (HS) or strength-hypertrophy-power (SHP) RT. In the present study, RT modified systemic inflammation measured as significant modifications in concentrations of selected cytokines. A primary finding was that the short-term initial phase of RT (4 wk) had significant effects on cytokines and adipocytokines: circulating pro-inflammatory resistin and MCP-1 concentrations increased, anti-inflammatory IL-1ra concentrations increased, and circulating leptin concentrations decreased along with the increasing muscle mass and decreasing fat mass. Furthermore, during the specialized RT periods, HS RT elicited normalizing effects on inflammation markers, such as circulating resistin and leptin. Also notable was the enhanced anti-inflammatory effect of RT that was achieved without a concomitant loss in body mass. It is notable that RT elicited a beneficial effect on body composition as muscle mass increased and fat mass decreased significantly. Interestingly, these adjustments in body composition were observed already after 4 wks of training at the end of the initial phase of training. Later, both HS and SHP RT further increased muscle mass, but reduction in fat mass was observed only after HS RT whereas, in the control group, a significant increase in fat mass was observed. Finally, we report that decreases in abdominal fat mass seem to be associated with the magnitude of the reductions in leptin concentrations.

Adipocytokines (also referred as adipokines) adiponectin, leptin, and resistin, are hormones that were initially found to be secreted by adipocytes and to regulate energy metabolism linking nutritional status to neuroendocrine function (Ouchi et al. 2011). Resistin stimulates the production of pro-inflammatory cytokines, and has been associated with obesity and atherosclerosis (Zhang et al. 2010) and several other diseases (Cao 2014). In the present study, we observed an increase in circulating resistin concentrations during the initial phase of RT, despite reductions in total and abdominal fat mass. However, muscle mass and muscle strength were increased. Our observation of increased circulating resistin concentrations could be due to the increased secretion of resistin by the activated anti-inflammatory macrophages in muscle

tissue (Schwartz and Lazar 2011, Filková et al. 2013). It has been shown that unaccustomed exercise leads to muscle damage characterized by transient ultrastructural myofibrillar distribution (Clarkson and Hubal. 2002, Pillon et al. 2013). Exercise-induced muscle damage initiates tissue repair and remodeling, which leads to the accumulation of inflammatory cells, including macrophages, into the muscle tissue. The activated macrophages, depending on their type, secrete pro-inflammatory and anti-inflammatory cytokines, which are needed for the regulation of muscle adaptations after exercise. (Hyldahl and Hubal 2014, Peake et al. 2017). The increased resistin concentrations in the present study could be due to macrophage activation and could be part of the efficient inflammation resolving process that has been shown to lead to regeneration of muscle fibers (Peake et al. 2017). Previous studies have demonstrated reduced resistin levels immediately after hypertrophic RT (Ihalainen et al. 2014, Varady et al. 2010). The present study found that during the specialized training period a significant reduction in resistin concentrations was observed only in the HS group. While speculative, we suggest that the new and unaccustomed training stimulus, explosive training, in the SHP program could have unbalanced the homeostasis of the body, which in turn induced muscle damage and elicit another initial response to a different stimulus.

Leptin is a pro-inflammatory hormone mainly secreted by adipocytes and acts as a peripheral signal informing the central nervous system of changes in the amount of adipose tissue in the body (Bouassida et al. 2010). In the present study, already 4 weeks of RT reduced circulating leptin concentrations in healthy young men. There was a correlation between the change in abdominal and total fat mass and reduction in leptin concentrations, which emphasizes the fact that changes in leptin levels seem to depend on a reduction in fat mass. It is possible that we did not observe significant reductions in leptin concentrations in the SHP group because fat mass was not reduced during training. The present study demonstrates that a significant reduction in body weight is not needed for a significant reduction in circulating leptin concentrations, although this study is in line with the previous studies, which have shown that a reduction in leptin is dependent on a reduction in fat mass (Baile et al. 2000). RT has been shown to favorably affect body composition (Kraemer et al. 2002). The effect of RT on body composition and inflammation markers seems to be strongly dependent on the intensity and external load of RT. In the beginning of the training, the beneficial effects in fat mass and leptin were observed with moderate intensity muscle endurance type

resistance training. However, for further improvements, more metabolically demanding HS training, with higher volume (repetitions  $\times$  load), slow velocity (longer muscle contraction), and shorter rest intervals than in SHP seems to be advantageous (Kraemer and Ratamess 2004).

An increase in MCP-1 concentrations was observed after four weeks of training. Later, both HS and SHP led to normalized MCP-1 concentrations. Thus, MCP-1 was significantly reduced after the specialized RT period in HS and SHP regardless of an absence of changes in fat mass in SHP. MCP-1 has been shown to increase after acute strenuous endurance type exercise (Suzuki et al. 2003), whereas a significant increase (Wells et al. 2016) or reduction (Ihalainen et al. 2014) has been observed after resistance exercise. Trosheid et al. (2004) suggested that especially visceral fat mass would have an effect on plasma levels of MCP-1. However, MCP-1 is also a potent chemotactic and activating factor for macrophages, inflammation, and skeletal muscle regeneration (Shireman et al. 2007). While speculative, the mechanism that could lead to higher MCP-1 concentration could be related to the muscle damage and the following muscle regeneration experienced during the initial phase of RT (Peake et al. 2005, Peake et al. 2017). Other mechanism that might lead increased MCP-1 concentrations after the initial phase of RT could be related to shear stress in vascular smooth muscle cells experienced in early phase of resistance training (Shyy et al. 1994). Nevertheless, more research is needed on the mechanisms that lead to higher circulating MCP-1 concentrations in the initial phase of RT. Furthermore, long-term resistance training seems to elicit a beneficial reduction in circulating MCP-1 concentrations as at the end of the study, after 12 weeks of specialized RT, a reduction in MCP-1 was observed in both training groups. The results of the present study suggest that changes in circulating MCP-1 concentrations are not entirely dependent on changes in adipose tissue mass.

In the present study a significant increase in IL-1ra, which is known to inhibit the pro-inflammatory response, was observed already after the first four weeks of training. Previously Lancaster & Febbraio (2014) suggested that the anti-inflammatory effect of exercise would be elicited by the release of IL-6 from skeletal muscle and subsequent production of IL-1ra by monocytes and macrophages. The previous studies on circulating IL-1ra and resistance exercise studies report on the acute effect of exercise, rather than on

basal levels (Peake et al. 2005, Izquierdo et al. 2009). Recently, Forti et al. (2017) showed that training only with high external load increases the basal levels of IL-1ra. Even if the RT program during the HS and SHP was progressive, it might be that it was not sufficient to elicit a significant response in IL-1ra.

**Limitations of the study.** The strength of this study is its prolonged randomized design training intervention. In addition, this study showed how starting RT affects the inflammation status and further compared the effects of two progressive and specific RT program on inflammation markers. Despite these strengths, our study has some limitations. First, the participants in this study were young healthy adults and therefore the results may not be applicable to other populations. Second, nutritional status has been shown to affect inflammation status. We followed the dietary intake of participants only once during the 16 weeks of training. Thus, we cannot rule out the effect of nutritional alterations on the present results, however, subjects were instructed to maintain their normal diet throughout the study. In addition, subjects received a post-exercise supplement that included carbohydrates, whey, or whey and carbohydrates. It has been suggested that whey could produce an anti-inflammatory effect (Krissansen 2007). However, due to a careful randomization and such a large n-size we found it improbable that there would be a consistent difference due to the supplements between the training groups. Lastly, although in the present study several different factors are suggested to be important markers and/or regulators of inflammation, there are many other pro- or anti-inflammatory factors that could be measured.

## Summary and Conclusion

In the present study, we show an overall anti-inflammatory effect of RT in healthy, young previously untrained men. Circulating leptin concentrations as well as total and abdominal fat mass decreased and IL-1ra increased already after four weeks of RT. Interestingly, we also observed increased circulating resistin and MCP-1 concentrations after 4 wk of RT, and those reduced towards their initial levels during prolonged RT probably as a consequence of muscle adaptation and regeneration. When aiming for reductions in abdominal fat mass and a more favorable inflammation status, metabolically more demanding RT, e.g. hypertrophic type of training should be preferred over strength and power type of RT.



## **Acknowledgements**

This work was supported by Tekes-National Technology Agency of Finland with University of Jyväskylä (Decision No. 70007/13), Juho Vainio Foundation, Ellen and Artturi Nyysönen Foundation, the Department of Biology of Physical Activity, University of Jyväskylä, and the competitive research funding of Pirkanmaa Hospital District. The authors would like to thank the subjects and research assistants. For ELISA analyses the excellent technical assistance of Terhi Salonen and Heini Brander is greatly acknowledged.

## **Conflict of interest statement**

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the manuscript.

## References

- Ara, I., Pérez-Gómez, J., Vicente-Rodriguez, G., Chavarren, J., Dorado, C., Calbet, J.A. 2006. Serum free testosterone, leptin and soluble leptin receptor changes in a 6-week strength-training programme. *Br. J. Nutr.* 96 (06): 1053-1059. doi: 10.1017/BJN20061956
- Baile, C.A., Della-Fera, M.A., Martin, R.J. 2000. Regulation of metabolism and body fat mass by leptin. *Annu. Rev. Nutr.* 20 (1): 105-127. doi: 10.1146/annure.nutr.20.1.105.
- Bouassida, A., Chamari, K., Zaouali, M., Feki, Y., Zbidi, A., Tabka, Z. 2010. Review on leptin and adiponectin responses and adaptations to acute and chronic exercise. *Br. J. Sports Med.* 44(9): 620-630. doi: 10.1136/bjism.2008.046151.
- Cao, H. 2014. Adipocytokines in obesity and metabolic disease. *J. Endocrinol.* 220(2): T47-59. doi: 10.1530/JOE-13-0339.
- Clarkson, P.M., and Hubal, M.J. 2002. Exercise-induced muscle damage in humans. *Am. J. Phys. Med. Rehabil.* 81(11): 52-69. doi: 10.1097/01.PHM.0000029772.45258.43
- Conraads, V.M., Beckers, P., Bosmans, J., De Clerck, L.S., Stevens, W.J., Vrints, C.J., Brutsaert, D.L. 2002. Combined endurance/resistance training reduces plasma TNF-alpha receptor levels in patients with chronic heart failure and coronary artery disease. *Eur. Heart J.* 23(23): 1854-1860.
- Fatouros, I.G., Chatzinikolaou, A., Tournis, S., Nikolaidis, M.G., Jamurtas, A.Z., Douroudos, I.I., Papassotiriou, I., Thomakos, P.M., Taxildaris, K., Mastorakos, G., Mitrakou, A. 2009. Intensity of resistance exercise determines adipokine and resting energy expenditure responses in overweight elderly individuals. *Diabetes Care*, 32 (12): 2161-2167. doi: 10.2337/dc08-1994.
- Filková, M., Šenolt, L., Vencovský, J. 2013. The role of resistin in inflammatory myopathies. *Curr. Rheumatol. Rep.* 15 (6): 1-7. doi: 10.1007/s11926-013-0336-0.

Forti, L.N., Van Roie, E., Njemini, R., Coudyzer, W., Beyer, I., Delecluse, C., Bautmans, I. . 2017. Effects of resistance training at different loads on inflammatory markers in young adults. *Eur. J. Appl. Physiol.* 117, 511–519. doi: 10.1007/s00421-017-3548-6.

Freidenreich, D.J. and Volek, J.S. 2012. Immune Responses to Resistance Exercise. *Exerc. Immunol. Rev.* 18 8-41.

Gleeson, M., Bishop, N.C., Stensel, D.J., Lindley, M.R., Mastana, S.S., Nimmo, M.A. 2011. The anti-inflammatory effects of exercise: mechanisms and implications for the prevention and treatment of disease. *Nature reviews. Immunology*, 11(9): 607-615. doi: 10.1038/nri3041.

Hansson, G. K. 2005. Inflammation, atherosclerosis, and coronary artery disease. *New England Journal of Medicine*, 352(16), 1685-1695.

Hulmi, J.J., Laakso, M., Mero, A.A., Häkkinen, K., Ahtiainen, J.P., Peltonen, H. 2015. The effects of whey protein with or without carbohydrates on resistance training adaptations. *Journal of the International Society of Sports Nutrition*, 12(1): 1-13. doi: 10.1186/s12970-015-0109-4.

Hyldahl, R.D., and Hubal, M.J. 2014. Lengthening our perspective: morphological, cellular, and molecular responses to eccentric exercise. *Muscle Nerve*, 49(2): 155-170. doi: 10.1002/mus.24077.

Ihalainen, J.K., Ahtiainen, J.P., Walker, S., Paulsen, G., Selänne, H., Härmäläinen, M., Moilanen, E., Peltonen, H., Mero, A.A. 2017. Resistance training status modifies inflammatory response to explosive and hypertrophic resistance exercise bouts. *J. Physiol. Biochem.* 1-10. doi: 10.1007/s13105-017-0590-0.

Ihalainen, J., Walker, S., Paulsen, G., Häkkinen, K., Kraemer, W.J., Härmäläinen, M., Vuolteenaho, K., Moilanen, E., Mero, A.A. 2014. Acute leukocyte, cytokine and adipocytokine responses to maximal and hypertrophic resistance exercise bouts. *Eur. J. Appl. Physiol.* 114(12): 2607-2616. doi: 10.1007/s00421-014-2979-6.

Izquierdo, M., Ibañez, J., Calbet, J.A., Navarro-Amezqueta, I., González-Izal, M., Idoate, F., Häkkinen, K., Kraemer, W.J., Palacios-Sarrasqueta, M., Almar, M. 2009. Cytokine and hormone responses to resistance training. *Eur. J. Appl. Physiol.* 107(4): 397-409. doi: 10.1007/s00421-009-1139-x.

Kraemer, W.J., and Ratamess, N.A. 2004. Fundamentals of resistance training: progression and exercise prescription. *Med. Sci. Sports Exerc.* 36(4): 674-688.

Kraemer, W.J., Ratamess, N.A., French, D.N. 2002. Resistance training for health and performance. *Current sports medicine reports*, 1(3): 165-171.

Krissansen, G.W. 2007. Emerging health properties of whey proteins and their clinical implications. *J. Am. Coll. Nutr.* 26(6): 713S-723S.

Lancaster, G.I., and Febbraio, M.A. 2014. The immunomodulating role of exercise in metabolic disease. *Trends Immunol.* 35(6): 262-269. doi: 10.1016/j.it.2014.02.008.

Libardi, C.A., De Souza, G.V., Cavaglieri, C.R., Madruga, V.A., Chacon-Mikahil, M. 2012. Effect of resistance, endurance, and concurrent training on TNF- $\alpha$ , IL-6, and CRP. *Med. Sci. Sports Exerc.* 44 50-56. doi: 10.1249/MSS.0b013e318229d2e9.

Moraes, C., Marinho, S.M., Da Nobrega, A.C., de Oliveira Bessa, B., Jacobson, L.V., Stockler-Pinto, M.B., Da Silva, W.S., Mafra, D. 2014. Resistance exercise: a strategy to attenuate inflammation and protein-energy wasting in hemodialysis patients? *Int. Urol. Nephrol.* 46(8): 1655-1662. doi: 10.1007/s11255-014-0712-3.

Murton, A.J., Billeter, R., Stephens, F.B., Des Etages, S.G., Graber, F., Hill, R.J., Marimuthu, K., Greenhaff, P.L. 2014. Transient transcriptional events in human skeletal muscle at the outset of concentric resistance exercise training. *J. Appl. Physiol.* 116(1): 113-125. doi: 10.1152/jappphysiol.00426.2013.

Olson, T.P., Dengel, D., Leon, A., Schmitz, K. 2007. Changes in inflammatory biomarkers following one-year of moderate resistance training in overweight women. *Int. J. Obes.* 31(6): 996-1003. doi: 10.1038/sj.ijo.0803534.

Ouchi, N., Parker, J.L., Lugus, J.J., Walsh, K. 2011. Adipokines in inflammation and metabolic disease. *Nature reviews. Immunology*, 11(2): 85-97.

Peake, J.M., Suzuki, K., Hordern, M., Wilson, G., Nosaka, K., Coombes, J.S. 2005. Plasma cytokine changes in relation to exercise intensity and muscle damage. *Eur. J. Appl. Physiol.* 95(5-6): 514-521. doi: 10.1007/s00421-005-0035-2.

Peake, J.M., Neubauer, O., Della Gatta, P.A., Nosaka, K. 2017. Muscle damage and inflammation during recovery from exercise. *J. Appl. Physiol.* 122(3): 559-570. doi: 10.1152/jappphysiol.00971.2016.

Petersen, A.M.W., and Pedersen, B.K. 2005. The anti-inflammatory effect of exercise. *J. Appl. Physiol.* 98(4): 1154-1162.

Phillips, M.D., Patrizi, R.M., Cheek, D.J., Wooten, J.S., Barbee, J.J., Mitchell, J.B. 2012. Resistance training reduces subclinical inflammation in obese, postmenopausal women. *Med. Sci. Sports Exerc.* 44(11): 2099-2110. doi: 10.1249/MSS.0b013e3182644984.

Pillon, N.J., Bilan, P.J., Fink, L.N., Klip, A. 2013. Cross-talk between skeletal muscle and immune cells: muscle-derived mediators and metabolic implications. *Am. J. Physiol. Endocrinol. Metab.* 304(5): E453-65. doi: 10.1152/ajpendo.00553.2012.

Pradhan, A.D., Manson, J.E., Rifai, N., Buring, J.E., Ridker, P.M. 2001. C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. *JAMA*, 286(3), 327-334.

Rall, L.C., Roubenoff, R., Cannon, J.G., Abad, L.W., Dinarello, C.A., Meydani S.N. 1996. Effects of progressive resistance training on immune response in aging and chronic inflammation. *Med. Sci. Sports Exerc.* 28(11): 1356-1365.

- Robinson, L.E., and Graham, T.E. 2004. Metabolic syndrome, a cardiovascular disease risk factor: role of adipocytokines and impact of diet and physical activity. *Canadian Journal of Applied Physiology*, 29(6): 808-829.
- Schwartz, D.R., and Lazar, M.A. 2011. Human resistin: found in translation from mouse to man. 22(7): 259-265. *Trends in Endocrinology & Metabolism*, 22(7): 259-265. doi: 10.1016/j.tem.2011.03.005.
- Scotece, M., Conde, J., Vuolteenaho, K., Koskinen, A., López, V., Gómez-Reino, J., Lago, F., Moilanen, E., and Gualillo, O. 2014. Adipokines as drug targets in joint and bone disease. *Drug Discov. Today*, 19(3): 241-258. doi: 10.1016/j.drudis.2013.07.012.
- Shireman, P.K., Contreras-Shannon, V., Ochoa, O., Karia, B.P., Michalek, J.E., McManus, L.M. 2007. MCP-1 deficiency causes altered inflammation with impaired skeletal muscle regeneration. *J. Leukoc. Biol.* 81(3): 775-785. doi: 10.1189/jlb.0506356.
- Shyy, Y.J., Hsieh, H.J., Usami, S., Chien, S. 1994. Fluid shear stress induces a biphasic response of human monocyte chemotactic protein 1 gene expression in vascular endothelium. *Proceedings of the National Academy of Sciences*, 91(11): 4678-4682.
- Suzuki, K., Nakaji, S., Yamada, M., Liu, Q., Kurakake, S., Okamura, N., Kumae, T., Umeda, T., Sugawara, K. 2003. Impact of a competitive marathon race on systemic cytokine and neutrophil responses. *Med. Sci. Sports Exerc.* 35 348-55. doi: 10.1249/01.MSS.0000048861.57899.04.
- Tallroth, K., Kettunen, J.A., Kujala, U.M. 2013. Reproducibility of regional DEXA examinations of abdominal fat and lean tissue. *Obes. Facts*, 6(2): 203-210. doi: 10.1159/000348238.
- Troseid, M., Lappégard, K.T., Claudi, T., Damas, J.K., Morkrid, L., Brendberg, R., Mollnes, T.E. 2004. Exercise reduces plasma levels of the chemokines MCP-1 and IL-8 in subjects with the metabolic syndrome. *Eur. Heart J.* 25(4): 349-355. doi: 10.1016/j.ehj.2003.12.006.

Varady, K.A., Bhutani, S., Church, E.C., Phillips, S.A. 2010. Adipokine responses to acute resistance exercise in trained and untrained men. *Med. Sci. Sports Exerc.* 42(3): 456-462. doi: 10.1249/MSS.0b013e3181ba6dd3.

Wells, A.J., Hoffman, J.R., Jatner, A.R., Varanoske, A.N., Church, D.D., Mangine, G.T. 2016. Monocyte Recruitment following High-Intensity and High-Volume Resistance Exercise. *Med. Sci. Sports Exerc.* 48(6), pp.1169-1178.

Zhang, M.H., Na, B., Schiller, N.B., Whooley, M.A. 2010. Resistin, exercise capacity, and inducible ischemia in patients with stable coronary heart disease: data from the Heart and Soul study. *Atherosclerosis*, 213(2): 604-610. doi: 10.1016/j.atherosclerosis.2010.09.015.

**Table 1.** Effects of RT on the circulating levels of inflammatory markers \*: Significant within-group change from pre to wk4. #: Significant within-group change from wk4 to wk16,  $\alpha$ : significant between group difference. na= not analysed.

		<b>HS + SHP (n=68)</b>	<b>SH (n=37)</b>	<b>SHP (n=31)</b>	<b>C (n=14)</b>
hs-CRP (mg·L <sup>-1</sup> )	wk0	1.5 ± 0.1	1.4 ± 0.1	1.6 ± 0.2	1.9 ± 0.4
	wk4	1.7 ± 0.2	1.5 ± 0.2	1.9 ± 0.3	na
	wk16	1.5 ± 0.2	1.4 ± 0.2	1.7 ± 0.3	1.6 ± 0.5
MCP-1 (pg·mL <sup>-1</sup> )	wk0	248.1 ± 16.7	234.1 ± 21.1	250.0 ± 26.1	236.2 ± 23.6
	wk4	264.2 ± 16.8*	258.8 ± 22.5*	278.3 ± 21.2*	na
	wk16	233.8 ± 14.7#	233.7 ± 20.0#	239.1 ± 21.0#	224.1 ± 18.8
IL-6 (pg·mL <sup>-1</sup> )	wk0	1.1 ± 0.1	1.2 ± 0.2	1.0 ± 0.1	1.0 ± 0.1
	wk4	1.2 ± 0.2	1.4 ± 0.3	1.0 ± 0.1	na
	wk16	1.2 ± 0.2	1.3 ± 0.2	1.1 ± 0.2	1.0 ± 0.1
IL-1ra (pg·mL <sup>-1</sup> )	wk0	307.2 ± 19.0	292.2 ± 12.9	330.0 ± 39.0	323.2 ± 26.7
	wk4	361.1 ± 19.5***	352.1 ± 27.3*	377.2 ± 27.7*	na
	wk16	334.0 ± 17.4	312.1 ± 17.2	367.4 ± 31.6	298.1 ± 13.9
Adiponectin (µg·mL <sup>-1</sup> )	wk0	7.0 ± 0.3	7.5 ± 1.2	6.9 ± 0.4	9.6 ± 0.9
	wk4	6.8 ± 0.4	7.4 ± 0.5	6.2 ± 0.5	na
	wk16	6.5 ± 0.3	7.0 ± 0.5	5.8 ± 0.4	9.3 ± 1.0
Leptin (ng·mL <sup>-1</sup> )	wk0	6.8 ± 0.7	6.6 ± 0.7	7.3 ± 1.1	6.0 ± 0.8
	wk4	6.4 ± 0.5*	6.2 ± 0.7*	6.7 ± 0.9*	na
	wk16	6.2 ± 0.6	5.7 ± 0.7## $\alpha$	7.0 ± 1.0	6.3 ± 1.2
Resistin (ng·mL <sup>-1</sup> )	wk0	12.1 ± 0.5	11.8 ± 0.6*	12.5 ± 0.9	11.6 ± 1.1
	wk4	13.4 ± 0.7*	12.9 ± 0.7*	13.9 ± 1.2*	na
	wk16	12.2 ± 0.5	11.6 ± 0.6#	12.9 ± 1.0#	11.8 ± 1.2



**Table 2.** The effect of RT on 1RM and body composition. \*: Significant within-group change from pre to wk4. #: Significant within-group change from wk4 to wk16.

	wk0				wk4			wk16		
	HS + SHP	HS	SHP	C	HS + SHP	HS	SHP	HS	SHP	C
	(n=68)	(n=37)	(n=31)	(n=14)	(n=68)	(n=37)	(n=31)	(n=37)	(n=31)	(n=14)
<b>Physical fitness</b>										
1RM (kg)	210 ± 33.8	207 ± 35.1	213 ± 32.3	173 ± 29.3	224 ± 33.3***	222 ± 33.7***	226 ± 33.3***	244 ± 32.0###	251 ± 36.1###	180 ± 27.9
<b>Body Composition</b>										
Body Mass (kg)	83.2 ± 11.0	84.9 ± 11.1	81.1 ± 10.9	80.7 ± 13.4	83.5 ± 10.8	84.9 ± 11.9	81.6 ± 10.5	84.9 ± 10.7	81.9 ± 10.6	81.7 ± 13.6
BMI (kg·m <sup>-2</sup> )	25.8 ± 3.2	25.8 ± 3.1	25.7 ± 3.3	25.2 ± 4.5	25.9 ± 3.2	25.9 ± 3.2	25.9 ± 3.2	25.2 ± 4.5	26.0 ± 3.2	25.5 ± 4.5
Body Fat Mass (kg)	20.4 ± 9.0	20.9 ± 8.5	20.1 ± 9.5	19.2 ± 8.9	19.8 ± 9.0***	20.2 ± 8.5***	19.7 ± 9.1***	18.9 ± 8.4###	19.4 ± 9.1	20.3 ± 9.1#
Body Fat Percentage (%)	23.8 ± 8.1	24.0 ± 7.3	23.5 ± 7.4	24.7 ± 8.5	22.7 ± 8.1***	23.2 ± 7.4***	22.1 ± 9.8***	21.7 ± 7.4###	21.8 ± 9.4	25.8 ± 9.3#
Abdominal Fat Mass (kg)	3.1 ± 1.6	3.2 ± 1.5	3.2 ± 1.8	2.4 ± 1.2	2.9 ± 1.6***	3.0 ± 1.5***	2.9 ± 1.8***	2.8 ± 1.5###	3.0 ± 1.7	2.6 ± 1.2#
Lean Mass (kg)	59.5 ± 5.9	60.5 ± 6.0	57.8 ± 4.9	59.6 ± 5.9	60.3 ± 6.1***	61.3 ± 6.1***	58.6 ± 5.1***	62.5 ± 6.1###	59.1 ± 5.0###	59.6 ± 5.9

## Figure caption

**Figure 1.** Effects of of RT on IL-1ra, MCP-1, resistin and leptin. \*: Significant within-group change from pre to wk4. #: Significant within-group change from wk4 to wk16, □: significant between group difference.

